

Substitution Form PTO-1449 (Modified) Information Disclosure Statement by Applicant (Use several sheets if necessary) AUG 06 2004 37 CFR § 1.98(b)	U.S. Department of Commerce Patent and Trademark Office		Attorney's Docket No. 14620-017001	Application No. 09/971,852
	Applicant Andres Francesch et al.			
	Filing Date October 3, 2001		Group Art Unit 1651	

U.S. Patent Documents

Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
126	AA	5,089,273	02/18/1992	Rinehart et al.	424	520	
	AB	5,149,804	09/22/1992	Rinehart et al.	540	466	
	AC	5,256,663	10/26/1993	Rinehart et al.	514	250	
	AD	5,478,932	12/26/1995	Rinehart et al.	540	466	
	AE	5,654,426	08/05/1997	Rinehart et al.	540	466	
	AF	5,721,362	02/24/1998	Corey et al.	540	466	
	AG	5,985,876	11/16/1999	Rinehart et al.	514	250	
	AH	6,124,292	09/26/2000	Corey	514	250	
	AI	6,316,214	11/13/2001	Rinehart et al.	435	25	
	AJ	6,348,467	02/19/2002	Corey	514	250	
	AK	6,686,470	02/03/2004	Danishefsky et al.	544	338	
	AL	2003/0216397	11/20/2003	Flores et al.	514	249	
✓	AM	2004/0002602 A1	01/01/2004	Francesch et al.	540	453	
	AN	2004/0019056	01/29/2004	Manzanares et al.	514	249	

Foreign Patent Documents or Published Foreign Patent Applications

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
126	AO	0 309 477 B1	11/06/1991	EPO	C07G	11/00		
	AP	59-225189	12/18/1984	Japan	C07D	471/18	Abstract	
	AQ	60-84288	05/13/1985	Japan	C07D	471/08	Abstract	
	AR	WO 87/07610	12/17/1987	WIPO	C07G	11/00		
	AS	WO 92/09607	06/11/1992	WIPO	C07D	515/22		
	AT	WO 98/12198	03/26/1998	WIPO	C07D	491/12		
	AU	WO 98/46080	10/22/1998	WIPO	A01N	43/58		
	AV	WO 99/58125	11/18/1999	WIPO	A61K	31/36		
	AW	WO 00/18233	04/06/2000	WIPO	A01N	43/58		
✓	AX	WO 00/69862	11/23/2000	WIPO	C07D	515/00		

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Foreign Patent Documents or Published Foreign Patent Applications

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<i>RG</i>	AY	WO 01/77115	10/18/2001	WIPO	C07D	515/22		
<i>1</i>	AZ	WO 01/87894	11/22/2001	WIPO	C07D	515/22		
<i>1</i>	AAA	WO 01/87895	11/22/2001	WIPO				

Other Documents (include Author, Title, Date, and Place of Publication)

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<i>RG</i>	ABB	Arai, T. et al., "The Structure of a Novel Antitumor Antibiotic, Saframycin A", <u>Experientia</u> , Vol. 36, pp. 1025-1027 (1980)
	ACC	Arai, Tadashi et al., "Increased Production of Saframycin A and Isolation of Saframycin S", <u>The Journal of Antibiotics</u> , Vol. XXXIII, No. 9, pp. 951-960 (1980)
	ADD	Arai, Tadashi et al., "Directed Biosynthesis of New Saframycin Derivatives with Resting Cells of <i>Streptomyces lavendulae</i> ", <u>Antimicrobial Agents and Chemotherapy</u> , Vol. 28, No. 1, pp 5-11 (1985)
	AEE	Arai, Tadashi et al., "Isoquinolineinones from Actinomycetes and Sponges", <u>The Alkaloids Chemistry and Pharmacology</u> , Vol. XXI, pp. 56-100 (1983)
	AFF	Arai, Tadashi et al., "New Antibiotics, Saframycins A, B, C, D and E", <u>The Journal of Antibiotics</u> , Vol. XXX, No. 11, pp. 1015-1018 (1977)
	AGG	Arai, Tadashi et al., "Increased Production of Saframycin A and Isolation of Saframycin S", <u>The Journal of Antibiotics</u> , Vol. XXXIII, No. 9, pp. 951-960 (1980)
	AHH	Asaoka, Takemitsu et al., "A New Saframycin, Saframycin R", <u>The Journal of Antibiotics</u> , Vol. XXXV, No. 12, pp. 1708-1710 (1982)
	AII	Barton, Derek H.R. et al., "Synthesis and Properties of a Series of Sterically Hindered Guanidine Bases", <u>Journal of the Chemical Society Perkin Transactions I</u> , No. 9, pp. 2085-2090 (1982)
	AJJ	Brown, J.M., "NCI's Anticancer Drug Screening Program May Not Be Selecting for Clinically Active Compounds," <u>Oncol. Res.</u> 9(5):213-215 (1997)
	AKK	Cable, Karl M. et al., "The Biosynthesis of Tuberin from Tyrosine and Glycine; Observations on the Stereochemistry Associated with the Conversion of Glycine through Methylenetetrahydrofolate into Methenyltetrahydrofolate", <u>Journal of the Chemical Society Perkins Transactions I</u> , No. 7, pp. 1593-1598 (1987)
	ALL	Cooper, Raymond et al., "Structure of the Quinone Antibiotic EM5519 and the Behavior of Quinones in Fast Atom Bombardment Mass Spectrometry", <u>The Journal of Antibiotics</u> , Vol. XXXVIII, No. 1, pp. 24-30 (1985)
	AMM	Corey, E.J. et al., "Enantioselective Total Synthesis of Ecteinascidin 743", <u>Journal of the American Chemical Society</u> , Vol. 118, No. 38, pp. 9202-9203 (1996)
	ANN	Cuevas, Carmen et al., "Synthesis of Ecteinascidin ET-743 and Phthalascidin Pt-650 from Cyanosafracin B", <u>Organic Letters</u> , Vol. 2, No. 16, pp. 2545-2548 (2000)
	AOO	Draetta, G. and Pagano, M., "Annual Reports in Medicinal Chemistry, Vol. 31," Academic Press, San Diego, pp. 241-246 (1996)
<i>1</i>	APP	Eckhardt, S.G. et al., "Activity of ecteinascidin, a novel marine cytotoxic, against primary human tumor colony-forming units", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 37, #2791, pp. 409 (1996)

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<i>RG</i>	AQQ	Faircloth, G. et al., "Ecteinascidin-743 (ET743): in vitro (IVT) and in vivo (INV) Results in Tumor Models", <u>The European Journal of Cancer</u> , Vol. 32A, Supp. 1, #24 O, pp. S5 (1996)
	ARR	Flam, Faye, "Chemical Prospectors Scour the Seas for Promising Drugs", <u>Science</u> , Vol. 266, pp. 1324-1325 (1994)
	ASS	Frincke, James M. et al., "Antimicrobial Metabolites of the Sponge Reniera sp.", <u>Journal of the American Chemical Society</u> , Vol. 104, pp. 265-269 (1982)
	ATT	Fukuyama, Tohru et al., "Total Synthesis of (±)-Saframycin A", <u>Journal of American Chemical Society</u> , Vol. 112, pp. 3712-3713 (1990)
	AUU	Fukuyama, Tohru et al., "Stereocontrolled Total Synthesis of (±)-Saframycin B", <u>Journal of American Chemical Society</u> , Vol. 104, pp. 4957-4958 (1982)
	AVV	Garcia-Rocha, M. et al., "Characterisation of antimitotic products from marine organisms that disorganize the microtubule network: ecteinascidin 743, isohomohalichondrin-B and LL-15", <u>British Journal of Cancer</u> , Vol. 73, pp. 875-883 (1996)
	AWW	Goldwasser, F. et al. "Characterization of ecteinascidin 743-induced DNA damages in cells", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 39, #4066, pp. 598 (1998)
	AXX	Guan, Yue et al., "Molecular and Crystal Structures of Ecteinascidins: Potent Antitumor Compounds from the Caribbean Tunicate Ecteinascidia Turbinata", <u>Journal of Biomolecular Structure & Dynamics</u> , Vol. 10, No. 5, pp. 793-818 (1993)
	AYY	Gulavita, Nanda K., et al., "Antimicrobial Constituents of a Sponge-Nudibranch Pair from Sri Lanka", <u>Bioactive Compounds from Marine Organisms</u> , Oxford & IBH Publishing Co. Pvt. Ltd., pp. 229-233 (1991)
	AZZ	He, Hai-yin et al., "Renieramycins E and F from the Sponge Reniera sp.: Reassignment of the Stereochemistry of the Renieramycins", <u>The Journal of Organic Chemistry</u> , Vol. 54, No. 24, pp. 5822-5824 (1989)
	AAAA	Hendriks, H.R. et al., "High antitumor activity of ET743 in human tumor xenograft models", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 37, #2653, pp. 389 (1996)
	ABBB	Ikeda, Yoshifumi et al., "Safracins, New Antitumor Antibiotics I. Producing Organism, Fermentation and Isolation", <u>The Journal of Antibiotics</u> , Vol. XXXVI, No. 10, pp. 1279-1283 (1983)
	ACCC	Ikeda, Yoshifumi et al., "Safracins, New Antitumor Antibiotics I. Producing Organism, Fermentation and Isolation", <u>The Journal of Antibiotics</u> , Vol. XXXVI, No. 10, pp. 1284-1289 (1983)
	ADDD	Koenig, Karl E., "The Applicability of Asymmetric Homogeneous Catalytic Hydrogenation", <u>Asymmetric Synthesis</u> , Ed. Morrison, Academic Press, Inc., Orlando, FL, Vol. 5, pp. 71 (1985)
	AEEE	Kofron, William G. et al., "A Convenient Method for Estimation of Alkylolithium Concentrations", <u>The Journal of Organic Chemistry</u> , Vol. 41, No. 10, pp. 1879-1880 (1976)
	AFFF	Kubo, Akinori et al., "Structure of Saframycin D, A New Dimeric Isoquinolinequinone Antibiotic", <u>Chem. Pharm. Bull.</u> , Vol. 35, No. 1, pp. 440-442 (1987)
	AGGG	Kuffel, M.J. et al., "Cytochrome P450 catalyzed metabolism of Ecteinascidin 743 by rat and human liver microsomes", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 38, #4003, pp. 596 (1997)
	AHHH	Ito, Yoichiro, "High-Speed Countercurrent Chromatography", <u>Critical Reviews in Analytical Chemistry</u> , Vol. 17, No. 1, pp. 65-143 (1986)
	AIII	Lichter, W. et al., "Biological Activities Exerted by Extracts of Ecteinascidia Turbinata", <u>Food and Drugs from the Sea Proceedings</u> , pp. 117-127 (1972)

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RG	AJJJ	Lown, J. William et al., "Structure and Confirmation of Saframycin R Determined by High Field ¹ H and ¹³ C NMR and its Interactions with DNA in Soloution", <u>The Journal of Antibiotics</u> , Vol. XXXVI, No. 9, pp. 1184-1194 (1983)
	AKKK	Lown, J. William et al., "Molecular Mechanisms of Binding and Single-Strand Scission of Deoxyribonucleic Acid by the Antitumor Antibiotics Saframycins A and C", <u>Biochemistry</u> , Vol. 21, No. 3, pp. 419-428 (1982)
	ALLL	Martinez, Eduardo J. et al., "Phthalascidin, a synthetic antitumor agent with potency and mode of action comparable to ecteinascidin 743", <u>Chemistry</u> , Vol. 96, pp. 3496-3501 (1999)
	AMMM	Mikami, Yuzuru et al., "Structural Studies on Minor Components of Saframycin Group Antibiotics Saframycins F, G and H", <u>The Journal of Antibiotics</u> , Vol. XLI, No. 6, pp. 734-740 (1988)
	ANNN	Mirsalis, J.C. et al., "Toxicity of Ecteinascidin 743 in female Fischer-344 rats administered i.v. in a multiple-dose regimen", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 38, #2073, pp. 309 (1997)
	AOOO	Moore, B.M. et al., "The NMR model of an ecteinascidin 743-DNA adduct", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 38, #2105, pp. 314 (1997)
	APPP	Nakagawa, Masako et al., "Total Synthesis of (-)-Eudistomin L and (-)-Debromoeudistomin L", <u>Journal of the American Chemical Society</u> , Vol. 111, No. 7, pp. 2721-2722 (1989)
	AQQQ	Parulekar, A.H. et al., "Bioactivity and Chemical Ecology of Some Interdial Animals", <u>Bioactivity and Chemical Ecology</u> , pp. 29-35
	ARRR	Pommier, Yves et al., "DNA Sequence- and Structure-Selective Alkylation of Guanine N2 in the DNA Minor Groove by Ecteinascidin 743, a Potent Antitumor Compound from the Caribbean Tunicate Ecteinascidia Turbinata", <u>Biochemistry</u> , Vol. 35, pp. 13303-13309 (1996)
	ASSS	Pretsch et al., <u>Tables of Spectral Data for Structure Determination of Organic Compounds</u> , pp. H125 (1983)
	ATTT	Reid, Joel M. et al., "Preclinical pharmacology of ecteinascidin 729, a marine natural product with potent antitumor activity", <u>Cancer Chemotherapy and Pharmacology</u> , Vol. 38, No. 4, pp. 329-334 (1996)
	AUUU	Remers, William A., "Saframycins, Renieramycins, and Safracins", <u>The Chemistry of Antitumor Antibiotics</u> , Vol. 2, pp. 93-119 (1988)
	AVVV	Rinehart et al., "Novel Bioactive Natural Products from Marine Organisms", <u>Topics in Pharmaceutical Sciences 1989</u> , pp. 613-626, D.D. Breimer, D.J.A. Cromwelin, K.K. Midha, Eds., Amsterdam Medical Press B.V. Noordwijk, The Netherlands (1989)
	AWWW	Rinehart, Kenneth L. et al., "Applications of High-Resolution Tandem FAB Mass Spectrometry", <u>Biological Mass Spectrometry</u> , eds. Burlingame et al., Elsevier Amsterdam, pp. 233-258 (1990)
	AXXX	Rinehart, Kenneth L. et al., "Biologically active natural products", <u>Pure and Applied Chemistry</u> , Vol. 62, No. 7, pp. 1277-1280 (1990)
	AYYY	Rinehart, Kenneth L. et al., "Bioactive Compounds from Aquatic and Terrestrial Sources", <u>Journal of Natural Products</u> , Vol. 53, No. 4, pp. 771-792 (1990)
	AZZZ	Rinehart, Kenneth L., "Antitumor Compounds from Tunicates", <u>Medicinal Research Reviews</u> , Vol. 20, No. 1, pp. 1-27 (2000)
✓	AAAAA	Rinehart, Kenneth L. et al., "Ecteinascidins 729, 743, 759A, 759B, and 770: Potent Antitumor Agents from the Caribbean Tunicate Exteinascidia Turbinata", <u>The Journal of Organic Chemistry</u> , Vol. 55, No. 15, pp. 4512-4515 (1990)

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RG	ABBBB	Saito, Naoki et al., "Synthesis of Saframycins. 3. Preparation of a Key Tricyclic Lactam Intermediate to Saframycin A", <u>The Journal of Organic Chemistry</u> , Vol. 54, No. 22, pp. 5391-5395 (1989)
	ACCCC	Sakai, Ryuichi et al., "Ecteinascidins: Putative Biosynthetic Precursors and Absolute Stereochemistry", <u>Journal of the American Chemical Society</u> , Vol. 118, No. 38, pp. 9017-9023 (1996)
	ADDDD	Sakai, Ryuichi et al., "Additional antitumor ecteinascidins from a Caribbean tunicate: Crystal structures and activities in vivo", <u>Proceedings of the National Academy of Sciences</u> , Vol. 89, No. 23, pp. 11456-11460 (1992)
	AEEEE	Shamma, Maurice et al., <u>Carbon-13 NMR Shift Assignments of Amines and Alkaloids</u> , pp. 206 (1979)
	AFFFF	Still, W. Clark et al., "Rapid Chromatographic Technique for Preparative Separations with Moderate Resolution", <u>Journal of Organic Chemistry</u> , Vol. 43, No. 14, pp. 2923-2925 (1978)
	AGGGG	Takahaski, Katsuhiro, "New Antibiotics, Saframycins A, B, C, D and E", <u>The Journal of Antibiotics</u> , Vol. XXX, No. 11, pp. 1015-1018 (1977)
	AHHHH	Takahaski, Katsuhiro et al., "Microbial Conversion of Saframycin A to 25-Dihydrosafamycin A and 21-Decyano-25-Dihydrosafamycin A (25-Dihydrosafamycin B) and Their Biological Activities", <u>The Journal of Antibiotics</u> , Vol. XXXV, No. 2, pp. 196-202 (1982)
	AIIII	Trowitzsch-Kienast, Wolfram et al., "Isolierung und Strukturaufklärung der Saframycine Mx 1 und Mx 2, neue antitumor-aktive Antibiotika aus Myxococcus xanthus", <u>Liebigs Ann. Chem.</u> , Vol. XXXV, pp. 475-481 (1988)
	AJJJJ	Witten, Jane L. et al., "Structures of Two Cockroach Neuropeptides Assigned by Fast Atom bombardment Mass Spectrometry", <u>Biochemical and Biophysical Research Communications</u> , Vol. 124, No. 2, pp. 350-358 (1984)
	AKKKK	Wright, Amy E. et al., "Antitumor Tetrahydroisoquinoline Alkaloids from the Colonial Ascidian Ecteinascidia Turbinata", <u>The Journal of Organic Chemistry</u> , Vol. 55, No. 15, pp. 4508-4512 (1990)
	ALLLL	Yazawa, Katsukiyo et al., "Bioconversions of Saframycin A Specific to some Genera of Actinomycetes", <u>The Journal of Antibiotics</u> , Vol. XXXV, No. 7, pp. 915-917 (1982)
	AMMMM	Yazawa, Katsukiyo et al., "Isolation and Structural Elucidation of New Saframycins Y3, Yd-1, Yd-2, Ad-1, Y2b and Y2b-d", <u>The Journal of Antibiotics</u> , Vol. XXXIX, No. 12, pp. 1639-1650 (1986)
✓	ANNNN	Zmijewski, Milton J., Jr. et al., "The in vitro Interaction of Naphthyridinomycin with Deoxyribonucleic Acids", <u>Chemico-Biological Interactions</u> , Vol. 52, No. 3, pp. 361-375 (1985)

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